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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/745,667	02/19/99	JENSEN	P 65111.000002

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HM12/0803

EXAMINER	
LEFFERS JR,G	
ART UNIT	**PAPER NUMBER**
1636	9

DATE MAILED: 08/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/242,657	JENSEN ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *22* is/are allowed.

6)☐ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Receipt is acknowledged of applicants' amendment, filed 5/10/01 as Paper No. 17, in which applicants have submitted amendments to the specification to insert new sequence identifiers, a new copy of the sequence listing, a corresponding CRF and an attorney's statement regarding the sequence listing. Two amendments to claims were proposed in Paper No. 17 which were not entered. The amendments to the claims were not entered because the proposed amendments were directed toward claims which are not pending in the instant specification. Claims 24 and 53 are not pending in the instant application, nor is it clear from the claim language which claims the amendments may actually be intended to amend.

Receipt is also acknowledged of applicants' amendment, filed 9/28/00 as Paper No. 9, in which claims 1-19, 21 and 22 were amended. Claims 1-22 are pending in this application.

Any rejection of record in Paper No. 7 not addressed in this action has been withdrawn. It is noted that applicants' amendment of claims 1-2, 5-8 and 22 necessitated withdrawal of the rejection of these claims under 35 U.S.C. 102 as being anticipated by Nilsson et al (AD). Because the new rejections made in this action were necessitated by applicants' amendment of the claims in Paper No. 9, the instant action is FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-21 are drawn to a set of promoters suitable for optimizing expression of a gene in a selected organism or group of organisms, methods of construction of the set of promoter sequences and methods of using subsets of promoter sequences from the first set of promoter sequences. In each case, the claims comprise the limitation that the first set of promoter sequences, with respect to promoter strength for the gene, covers a range of promoter activities which is within a range from the weakest possible activity that is detectable to the strongest possible activity that is detectable. Assay conditions for detection of promoter activity are not specified in the claim language (e.g. which assay to use to measure promoter activity, assay conditions including assay temperature, in vitro versus in vivo, duration of the assay, inducible versus constitutive expression, etc.). Thus, each of the claims are drawn to an incredibly broad genus of possible sets of promoters driving the expression of <u>any</u> given gene in <u>any</u> possible organism under any set of conditions and measured with <u>any</u> assay that can possibly measure promoter activity. The breadth of the genus of sets of promoters encompassed by the rejected claims is further exacerbated by the functional limitation of encompassing both the weakest and the strongest detectable expression for the given gene in a given organism. Many of the claims further comprise the functional limitation that the range of promoter activity be spanned by members of the set of promoters in increments of activity that differ by 50-100% between "adjacent" members of the set of promoters.

The specification does not appear to provide even a single embodiment of the claimed invention wherein the set of promoters encompasses both the weakest and strongest detectable level of gene expression for a given gene in a given organism. The prior art does not appear to teach a set of promoters which meet the functional limitations with regard to range of expression for a given gene in a given organism.

Given the extreme scope of possible sets of promoters encompassed by the rejected claims wherein the set of promoters must encompass both the weakest and strongest levels of gene expression for any given gene under any given conditions and measured by any assay capable of determining gene expression levels, and given the lack of description of even one embodiment of the claimed invention within the specification or prior art, one of skill in the art would not be able to envision a representative number of embodiments of the claimed invention to describe the claimed genus of sets of promoters which are critical to applicants' invention. Therefore, one of skill in the art would reasonably conclude applicants were not in possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections, necessitated by applicants' amendment to the claims in Paper No. 9.**

Claims 1, 16 and 21 are vague and indefinite in that the metes and bounds of the phrase "...a range from the weakest possible activity that is detectable to the strongest

possible activity that is detectable..." are unclear. By what assay does one determine the weakest or strongest possible level of activity for expression of a gene under control of different promoters and under what assay conditions? The cited phrase is inherently indefinite, depending upon the assay chosen and the assay conditions under which the measurements of promoter activity are made (e.g. in vitro, in vivo, culture conditions, assay temperature, duration, etc.). It would be remedial to amend the claim language to more clearly indicate the range of expression activity required for a set of promoters to meet the claim limitations.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "...at least two consensus sequences, said at least two consensus sequences corresponding to conserved sequences identified in said organism or group of organisms, at least half of each of said consensus sequences being kept constant in the set of promoter sequences..." are unclear. What exactly is a "conserved" sequence? Does the term specify nucleic acid identity from species to species or does it allow for some sequence variation from example to example? If variation is allowed, how much variation is acceptable in order to meet the claim limitation? Across how many different organisms must the "conserved" sequence be identical? The phrase is also indefinite in that it is still unclear whether the phrase specifies that a set of nucleotides is kept constant throughout each conserved sequence or that each member of the set of promoter sequences need only have 50% identity to the conserved sequence. It would be remedial to amend the claim language to more clearly indicate what is intended by the terms "conserved sequence" and "consensus sequence".

Claims 1 and 16 are vague and indefinite in that the metes and bounds of the term "substantially random" incorporation of nucleotides are unclear. The term does not appear to be specifically defined in the specification. How random is "substantially" random incorporation of nucleotides in a given sequence?

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "...at least two consensus sequences, which consensus sequences correspond to conserved sequences identified in said organism or group of organisms..." are unclear. What exactly is a "conserved" sequence? Does the term specify nucleic acid identity from species to species or does it allow for some sequence variation from example to example? If variation is allowed, how much variation is acceptable in order to meet the claim limitation? Across how many different organisms must the "conserved" sequence be identical? It would be remedial to amend the claim language to more clearly indicate what is intended by the terms "conserved sequence" and "consensus sequence".

Claim 18 is vague and indefinite in that the metes and bounds of the phrase "desired range of promoter activities" are unclear. Likewise, the metes and bounds of the phrase "optimal level of gene expression" are unclear. The terms "desired range" and "optimal level" are inherently indefinite, having a definition that will vary from investigator to investigator and making it unclear as to which promoters and levels of gene expression are encompassed by the rejected claims. It would be remedial to amend the claim language to more clearly indicate what exactly constitutes a "desired range of activities" and an "optimal level of gene expression".

Claim 21 is vague and indefinite in that the metes and bounds of the phrase "optimal level of gene expression" are unclear. The term "optimal level" is inherently

indefinite, having a definition that will vary from investigator to investigator and making it unclear as to which promoters and levels of gene expression are encompassed by the rejected claims. It would be remedial to amend the claim language to more clearly indicate what exactly constitutes a "desired range of activities" and an "optimal level of gene expression".

Response to Arguments

Applicant's arguments filed 9/28/00 with regard to rejection of claims in Paper No. 7 for being indefinite with regard to the term "consensus sequence" have been fully considered but they are not persuasive. Applicants' response essentially argues that the term is well defined in the art and that one of skill in the art would know what is meant by the cited term. In support of applicants' argument the response submits a definition of the term "consensus sequence" obtained from the Oxford Dictionary of Biochemistry and Molecular Biology, Oxford University Press 1997, which is as follows: "an idealized sequence of nucleotides, or their constituent bases, or amino acids, base or amino acids, base or amino acid that represents the nucleotide most likely to occur at each position in the sequence. Consensus sequences are used to identify RNA splicing sites, other sites, plastids and families of proteins." This definition does not clarify the cited term in the context of the claimed invention. What exactly is an "idealized" sequence with regard to the instant invention and under what limitations is the "idealized" or "most likely" nucleotide to occur at each position of the "consensus" sequence to be determined? As indicated above, the added term of "conserved sequence" doesn't clarify the term "consensus sequence" and has many of the same issues as indicated for the term

"consensus sequence" regarding the parameters used for one to determine a given sequence is a "consensus sequence".

Conclusion

Claim 22, drawn towards a promoter sequence consisting of the nucleotide sequence described by one of the sequence identifiers selected from the group of SEQ ID NOS: 5-58, is allowed. Claims 1-21 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. §1.6(d)). The official fax telephone numbers for the

Group are (703) 308-4242 and (703) 305-3014. NOTE: If applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald Leffers , Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Rob Schwartzman, Ph.D., can be reached at (703) 308-7307.

Any inquiry of a general nature or relating to the status of this application, or relating to attachments to this office action, should be directed to the Patent Analyst Zeta Adams, whose telephone number is (703) 305-3291.

GLJ

G. Leffers Jr., Ph.D.

Patent Examiner

Art Unit 1636

13 July 2001

DAVID GUZO
PRIMARY EXAMINER